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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,194	06/30/2005	Bertus Noordam	GRT4662-45	8070
23117 7590 07/31/2008 NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203				
EXAMINER				
LAU, JONATHAN S				
ART UNIT		PAPER NUMBER		
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/541,194

**Applicant(s)**

NOORDAM ET AL.

**Examiner**

Jonathan S. Lau

**Art Unit**

1623

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 April 2008.  
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 6-15 and 20-30 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 6-15 and 20-30 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☐ Information Disclosure Statement(s) (PTO-8508)  
Paper No(s)/Mail Date \_\_\_\_\_  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_  
5) ☐ Notice of Informal Patent Application  
6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This Office Action is responsive to Applicant's Amendment and Remarks, filed 04 Apr 2008, in which claim 12 is amended to change the scope and breadth of the claim; new claim 30 is added; and claim 20 is amended to be written as an independent claim by reciting all the limitations of claim 6 from which claim 20 depended.

This application is the national stage entry of PCT/EP04/00658, filed 23 Jan 2004; and claims benefit of foreign priority document EPO 03075255.4, filed 27 Jan 2003. The foreign priority document is in English.

Claims 6-15 and 20-30 are pending in the current application.

### ***Objections Withdrawn***

Applicant's Amendment, filed 04 Apr 2008, with respect to objections to the specification has been fully considered and is persuasive, because it is now clear what text corresponds to which section of the specification.

This objection has been **withdrawn**.

### ***Rejections Withdrawn***

Applicant's Amendment, filed 04 Apr 2008, with respect to rejection of claims 6, 8-13 and 20-29 under 35 U.S.C. 103(a) as being unpatentable over Tanekawa et al. (US Patent 4,303,680, issued 1 Dec 1981, of record) in view of Keller et al. (US Patent 4,623,723, issued 18 Nov 1986, of record), with evidence provided by Kanegae et al.

(US Patent 4,810,509, issued 7 Mar 1989, of record) and Chae et al. (Bioresource Technology, 2001, 76, p253-258, of record), has been fully considered and is persuasive with regard to claim 12, because Tanekawa and Keller do not specifically disclose the RNA recovered in the filter's retentate as required by amended claim 12.

This rejection of claim 12 has been **withdrawn**.

The following new or modified rejections are necessitated by Applicant's Amendment, filed 04 Apr 2008, in which claim 12 is amended to change the scope and breadth of the claim; new claim 30 is added; and claim 20 is amended to be written as an independent claim by reciting all the limitations of claim 6 from which amended claim 20 previously depended.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 6, 8-13 and 20-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanekawa et al. (US Patent 4,303,680, issued 1 Dec 1981, of record) in view of Keller et al. (US Patent 4,623,723, issued 18 Nov 1986, of record), with evidence provided by Kanegae et al. (US Patent 4,810,509, issued 7 Mar 1989, of record) and Chae et al. (Bioresource Technology, 2001, 76, p253-258, of record).

Tanekawa et al. discloses a process for producing a flavoring composition containing 5'-ribonucleotides (column 2, lines 9-10) comprising (i) treating yeast cells to release cell contents comprising RNA (column 2, lines 13-16), (ii) extracting the RNA present in the released cell contents (column 2, lines 18-20), and (iii) converting the separated RNA into 5'-ribonucleotides (column 2, lines 21-25), meeting limitations of instant claim 6. Tanekawa et al. discloses treating the yeast cells to release cell contents comprising RNA by autolysis or hydrolysis using enzymes is a conventional method (column 1, lines 25-30), and Kanegae et al. explains that autolysis involves the action of proteases (Kanegae et al., column 3, line 39), meeting limitations of instant claims 8, 9 and 25. Tanekawa et al. discloses removal of insoluble solid material originating from the cells by methods such as centrifugation and filtration after extraction of RNA from the cell and prior to converting the separated RNA into 5'-ribonucleotides (column 4, lines 13-18), meeting limitations of instant claims 10 and 11. Tanekawa et al. discloses using a 5'-phosphodiesterase to hydrolyze the separated RNA into 5'-

Art Unit: 1623

nucleotides (column 4, lines 19-20) as well as deaminase (column 4, line 25), meeting limitations of instant claims 13, 26 and 27. Tanekawa et al. discloses the preferred yeast cells are *Saccharomyces cerevisiae* (column 3, lines 4-5), meeting limitations of instant claims 28 and 29. Tanekawa et al. discloses an example in which the composition produced comprises more 5'-GMP (0.78%) than the sum of 5'-IMP and 5'-AMP, enzymatically converted to 5'-IMP (0.7 %) (column 7, lines 38-40), meeting limitations of instant claim 24. Tanekawa et al. is silent as to the glutamate content of the yeast extract. Chae et al. explains that yeast extract prepared by a combination of protease, 5'-phosphodiesterase, and deaminase inherently contains 25.9% amino acids on a solid weight basis (Chae et al. page 257, left column, lines 26-29 and 33-35), and the amino acids composition is 7.80% glutamic acid (Chae et al. page 257, right column, table 3, entry "Glutamic acid"), giving a composition that comprises 2.02% w/w of glutamate, meeting limitations of instant claim 23.

Tanekawa et al. does not specifically disclose separating the RNA present in the released cell contents from other soluble cell material (instant claim 6 and 20, step (ii)) in the process of extracting the RNA present in the released cell contents (column 2, lines 13-16). Tanekawa et al. does not specifically disclose the removal of solid material originating from the cells prior to separating the RNA present in the released cell contents from other soluble cell material (instant claims 10 and 11). Tanekawa et al. does not disclose the process wherein the composition comprises at least 55% w/w of 5'-ribonucleotides (instant claim 20), at least 65% w/w of 5'-ribonucleotides (instant claim 21), or at least 75% w/w of 5'-ribonucleotides (instant claim 22). Tanekawa et al.

Art Unit: 1623

does not specifically disclose the RNA recovered in the filter's retentate (instant claim 12). Tanekawa et al. does not specifically disclose ultrafiltration by a filter having a molecular weight cut-off from 10 kD to 50 kD (instant claim 30).

Keller et al. teaches aqueous cell extracts containing nucleic acids (Keller et al. column 1, lines 5-17), corresponding to the RNA extract disclosed by Tanekawa et al., filtered to separate deoxyribonucleic acid in the nucleic acids solution from ribonucleic acid in the nucleic acids solution by an ultrafiltration process (Keller et al. column 2, lines 58-65), meeting limitations of step (ii) of instant claim 6 and instant claim 12. Example 8 in US Patent 4,206,243, referred to in Keller et al. column 2, lines 53-55 and excerpted here:

EXAMPLE 8

*Candida lipolytica* ATCC 20383, a hydrocarbon-utilizing yeast species, was cultivated on n-paraffins in the presence of an aqueous nutrient medium and an oxygen-containing gas. The yeast cell mass was separated from the nutrient solution and dried.

100 g of the dry yeast cell mass were suspended at room temperature under normal pressure in 300 g of methanol and 10 g of gaseous  $\text{NH}_3$  were added to this mixture within 15 minutes, the temperature of the suspension being maintained at 15° C. by cooling. After the gas was introduced, agitation was continued for another 20 minutes at 22° C., followed by filtration through a sucton frit. The filter cake was mixed once thoroughly on the frit with 300 ml of methanol, then vacuum filtered. The two filtrates were combined. The solution had a yellow color and contained the lipids of the originally used cell material. Methanol and  $\text{NH}_3$  were removed under reduced pressure (14 mm Hg).

The residue after the second filtration, consisting of the destroyed and degreased cells of the microorganism, was dried in a vacuum drying cabinet (100 mm Hg) at 40° C. for 5 hours. The thus obtained product exhibited a light color than the yeast cell mass originally used, and was odorless.

100 g of degreased and dried yeast were suspended in a solution of 1 liter of distilled water and 1000 ml of methanol, in order to reduce the original nucleic acid content of 7.5 weight %, calculated on the starting material. The mixture was agitated and, at a pH of 6.8, to which it adjusted itself, was heated to 50° C. for 15 minutes. Then by centrifugation it was separated into a sediment containing the yeast protein, and a liquid phase containing nucleic acid. The sediment was subjected to vacuum freeze drying after having been washed once more at room temperature.

The nucleic acid content of the dry material had diminished from the original 7.5 weight % to 0.4 weight %.

teaches the removal of solid material originating from the cells prior to the filtration taught by Keller et al., addressing instant claims 10 and 11. Keller et al. further teaches the isolation of the RNA (Keller et al. column 2, lines 45-49) to give a composition that is 100% 5'-ribonucleotides, meeting limitations of instant claims 20-22. Keller et al. also teaches the enzymatic degradation of the RNA-containing permeate without isolation to give the 5'-ribonucleotides (Keller et al. column 2, lines 3-8). Keller et al. teaches 5'-ribonucleotides used as foodstuff additives are obtained by treating the aqueous cell extracts containing nucleic acids with 5'-phosphodiesterase, and that the



Art Unit: 1623

5'-deoxynucleotides by-products produced by DNA reacting with 5'-phosphodiesterase are difficult to separate from the desired 5'-ribonucleotides (Keller et al. column 1, lines 18-27). Keller teaches "The exclusion limit of the membrane is selected to accord with the known or determined molecular weights of the nucleic acids to be separated" (column 1, lines 50-55) and that "Membrane separating processes are generally familiar and especially so in biotechnology" (column 1, lines 55-60).

It would have been obvious to one of ordinary skill in the art at the time of the invention to improve the process for producing a flavoring composition containing 5'-ribonucleotides disclosed by Tanekawa et al. with the known method taught by Keller et al. of separating the RNA present in the released cell contents from other soluble cell material. Both Tanekawa et al. and Keller et al. disclose production of 5'-ribonucleotides as a foodstuff additive, and Keller et al. teaches that it is desirable that the process be improved by separating the RNA present in the released cell contents from other soluble cell material prior to converting the separated RNA into 5'-ribonucleotides (Keller et al. column 1, lines 18-27). It would have been obvious to one of ordinary skill in the art to perform routine optimization of the range of the exclusion limit of the membrane because Keller teaches the exclusion limit of the membrane is selected to accord with the known or determined molecular weights of the nucleic acids to be separated. It would have been obvious to one of skill in the art to reverse parts of the membrane separating processes so that the RNA recovered in the filter's retentate instead of the filtrate, because the reversal of parts is an obvious expedient to one of ordinary skill in the art in isolating both the DNA and RNA as taught by Keller and

because Keller teaches membrane separating processes are generally familiar and especially so in biotechnology.

**Response to Applicant's Remarks:**

Applicant's Amendment and Remarks, filed 04 Apr 2008, have been fully considered and found not to be persuasive.

Applicant asserts that neither Tanekawa nor Keller separates RNA from soluble material in the cell extract having a smaller or the same size as the RNA. However, this specific limitation is not found in the instant claims. Keller teaches separating the RNA from DNA, a soluble cell material present in the liquid phase (Keller, column 2, lines 30-35), meeting the limitation of step (ii) in instant claims 6 and 20.

Applicant asserts that the recitation of the limitation of "Tanekawa et al. does not disclose the process wherein the composition comprises at least 75% w/w of 5'-ribonucleotides (instant claims 20-22)." is in error. It is noted that a method meeting the limitation of "at least 75% w/w of 5'-nucleotides" (instant claim 22) necessarily meets the limitation of "at least 55% w/w of 5'-nucleotides" (instant claim 20) and "at least 65% w/w of 5'-nucleotides" (instant claim 21). However, for clarity the limitations of instant claims 20, 21 and 22 are explicitly stated in the rejection above. The grounds of rejection are not changed.

Applicant asserts that 5'-ribonucleotides are mononucleotides distinct from the polynucleotides of RNA, and therefore not contained in the composition taught by Keller. However, as recited above, Keller et al. also teaches the enzymatic degradation of the RNA-containing permeate without isolation to give the 5'-ribonucleotides (Keller et

al. column 2, lines 3-8). Therefore the teaching of Keller clearly leads one of ordinary skill in the art to the composition containing 5'-ribonucleotides.

Claim 6, 7 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanekawa et al. (US Patent 4,303,680, issued 1 Dec 1981, of record) in view of Keller et al. (US Patent 4,623,723, issued 18 Nov 1986, of record) as applied to claims 6, 8-13 and 20-29 above, and further in view of Potman et al. (US Patent 5,288,509, issued 22 Feb 1994, of record).

Tanekawa et al. in view of Keller et al. render unpatentable a process for producing a flavoring composition containing 5'-ribonucleotides (column 2, lines 9-10) comprising (i) treating yeast cells to release cell contents comprising RNA (Tanekawa et al. column 2, lines 13-16), (ii) separating the RNA present in the released cell contents from other soluble cell material (Keller et al. column 2, lines 58-65), and (iii) converting the separated RNA into 5'-ribonucleotides (Tanekawa et al. column 2, lines 21-25).

Tanekawa et al. in view of Keller et al. does not disclose the process wherein the native enzymes of the cell are inactivated prior to treating the cells to release the cell contents (instant claim 7).

Potman et al. teaches the process for preparing a yeast extract useful as a food flavor (Potman et al., abstract), involving the deactivation of the native enzymes of the yeast (Potman et al. column 2, lines 32-36) prior to the enzymatic degradation of the cell with a protease such as papain (Potman et al. example 1 on column 5, lines 6-14).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute functional equivalent methods of enzymatic degradation of the cell to practice the invention of Tanekawa et al. in view of Keller et al. with the method involving the deactivation of the native enzymes of the yeast prior to the enzymatic degradation of the cell with an exogenous protease such as papain taught by Potman et al. in place of autolysis with the cell's endogenous protease with a reasonable expectation of success. Tanekawa et al. discloses treating the yeast cells to release cell contents comprising RNA by autolysis or hydrolysis using enzymes is a conventional method (Tanekawa et al. column 1, lines 25-30). Potman et al. teaches the equivalence of enzymatic degradation of the cell with an exogenous protease and autolysis with the cell's endogenous protease (Potman et al., column 2, lines 45-50).

**Response to Applicant's Remarks:**

Applicant's Amendment and Remarks, filed 04 Apr 2008, have been fully considered and found not to be persuasive.

The response to Applicant's remarks regarding Tanegawa in view of Keller are as recited above.

Claims 6, 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanekawa et al. (US Patent 4,303,680, issued 1 Dec 1981, of record) in view of Keller et al. (US Patent 4,623,723, issued 18 Nov 1986, of record) as applied to claims 6, 8-13 and 20-29 above, and further in view of Tsuda et al. (US Patent 4,374,981, issued 22 Feb 1983, of record).

Tanekawa et al. in view of Keller et al. render unpatentable a process for producing a flavoring composition containing 5'-ribonucleotides (column 2, lines 9-10) comprising (i) treating yeast cells to release cell contents comprising RNA (Tanekawa et al. column 2, lines 13-16), (ii) separating the RNA present in the released cell contents from other soluble cell material (Keller et al. column 2, lines 58-65), and (iii) converting the separated RNA into 5'-ribonucleotides (Tanekawa et al. column 2, lines 21-25).

Tanekawa et al. in view of Keller et al. does not disclose the process wherein the 5'-ribonucleotides are further purified by removal of compounds having a higher molecular weight (instant claim 14) by ultrafiltration (instant claim 15).

Tsuda et al. discloses the separation of inosine and/or guanosine by ultrafiltration of fermentation broth to remove high molecular weight substances (Tsuda et al. column 2, lines 9-15). Tsuda et al. teaches ultrafiltration is a useful method to remove both suspended solids and also soluble, high molecular weight contaminants (Tsuda et al. column 1, lines 19-30). Tsuda et al. teaches that ultrafiltration is a useful method for separating inosine and guanosine, useful as starting substances for a flavor nucleotide, from a fermentation broth, or cellular extract, containing such substances (Tsuda et al. column 1, lines 35-39).

It would have been obvious to one of ordinary skill in the art at the time of the invention to improve the invention of Tanekawa et al. in view of Keller et al. by using the known technique of Tsuda et al. to improve a similar method in the same way because of the teaching of Tsuda et al. that ultrafiltration is a useful method to remove both suspended solids and also soluble, high molecular weight contaminants (Tsuda et al.

Art Unit: 1623

column 1, lines 19-30). Tanekawa et al. discloses a yeast extract containing flavoring nucleotides (Tanekawa et al. column 2, lines 9-10). Tsuda et al. teaches that ultrafiltration is a useful method for separating inosine and guanosine, useful as starting substances for a flavor nucleotide, from a fermentation broth, or cellular extract, containing such substances (Tsuda et al. column 1, lines 35-39). A nucleotide is a nucleoside that is phosphorylated and has a similarly low molecular weight compared to high molecular weight contaminants, and with regard to the molecular-weight based filtration methods of Tsuda et al. is a functional equivalent. Therefore to improve the invention of Tanekawa et al. in view of Keller et al. by using the known technique of Tsuda et al. to improve a similar method would have been obvious to one of ordinary skill in the art at the time of the invention.

**Response to Applicant's Remarks:**

Applicant's Amendment and Remarks, filed 04 Apr 2008, have been fully considered and found not to be persuasive.

The response to Applicant's remarks regarding Tanegawa in view of Keller are as recited above.

***Conclusion***

No claim is found to be allowable.

Applicant's amendment necessitated the new and modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See

MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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